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PHARMACOGENOMICS IN PERSONALISED MEDICINE: CURRENT ADVANCES AND CLINICAL APPLICATIONS

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Pharmacogenomics links genetic variation with variability in drug response and has become an essential component of personalised medicine aimed at improving therapeutic efficacy and reducing adverse drug reactions across clinical practice. Rapid advances in genomic technologies have generated extensive pharmacogenomic data; however, integration of this knowledge into routine medical decision-making remains uneven and fragmented across healthcare systems. This review aims to synthesise recent advances and clinical applications of pharmacogenomics across major therapeutic areas while highlighting barriers that influence its clinical implementation. Evidence indicates that pharmacogenomic markers significantly influence drug response in oncology, cardiovascular diseases, psychiatry, neurology, infectious diseases, pain management, and gastrointestinal disorders. Gene–drug associations involving CYP450 enzymes, HLA alleles, SLCO1B1, TPMT, and NUDT15 have improved prediction of treatment efficacy and risk of drug toxicity. Findings also indicate that pharmacogenomic testing supports individualised dosing strategies, targeted therapy selection, and improved patient safety in multiple clinical contexts. Clinical translation remains limited by economic barriers, insufficient clinician awareness, population diversity gaps, and challenges in interpreting complex genomic data. Continued expansion of genomic research, integration of pharmacogenomic data into clinical decision systems, and development of standardised guidelines may strengthen clinical adoption. Pharmacogenomics represents a critical pathway toward safer, more effective, and individualised pharmacotherapy in modern healthcare systems.

Keywords*: Pharmacogenomics, Precision medicine, Personalised therapy, Pharmacogenetics, Drug response*

Introduction

Pharmacogenomics has become a core field of precision medicine in areas where correlation is made between the variability of genomic sequence or genetic data and the variability in response to a drug, in order to design an individualised therapeutic strategy, thereby making the treatment safer and more effective (Sadee et al., 2023). The concept derives from pharmacogenetics, which proved that inherited genetic polymorphisms affect drug metabolism, transport and pharmacological targets, resulting in comparable variable therapeutic outcomes among patients who are treated with the same medication (Valdes & Yin, 2016). As genomic technologies have improved, pharmacogenomics has moved from single-gene studies to analyses using genome-wide association (GWa), which investigates complex networks of genetic factors that modulate pharmacokinetics and pharmacodynamics (Cecchin & Stocco, 2020). These developments have enhanced the role of genomics and clinical decision making, stimulating the incorporation of genetic information in the choice of therapy and its dosage (Cascorbi, 2018). Interindividual variability in drug response can be a great challenge in medicine because, unsurprisingly, standard treatment regimens do not always take into account the genetic variation of the patients (Chenoweth et al., 2020). Consequently, adverse drug reactions continue to be a significant problem for healthcare worldwide, leading to higher hospitalisation rates, morbidity, and healthcare costs in numerous clinical settings (Chenoweth et al., 2020). The development of new digitised genomic technologies, such as next-generation sequencing and genome-wide association studies, has accelerated the identification of pharmacogenomic biomarkers that are linked to therapeutic response (Morganti et al., 2019). These advancements have revolutionised drug development and clinical therapeutics, as they have allowed more accurate identification of patient subgroups that will likely benefit from specific pharmacological interventions (Mirsadeghi & Larijani, 2017).

In oncology, several examples of the central role of pharmacogenomic biomarkers are in the guiding of targeted therapies by identifying tumour-specific genetic alterations that predict sensitivity or resistance to anticancer agents (Camidge et al., 2019). Molecular testing for oncogenic mutations has made significant contributions to treating patients because it now helps clinicians to link targeted therapies for certain genetic profiles of tumours (Piawah & Venook, 2019). Similarly, cardiovascular pharmacogenomics has shown that genetic polymorphisms on enzymes such as CYP2C19 play a significant role in the response of patients to antiplatelet therapy such as clopidogrel (Brown & Pereira, 2018). Genetic differences that can influence anticoagulant metabolism also have an impact on the dosing requirements of warfarin, so pharmacogenomics-based therapeutic algorithms are an important part of cardiovascular medicine (Asiimwe et al., 2021). In psychiatric medicine, pharmacogenomic studies have demonstrated that metabolic variations in genes that encode enzymes in the cytochrome P450 family influence the metabolism of antidepressants and antipsychotics, which can influence therapeutic response and adverse drug reactions (Pardiñas et al., 2021). Genetic factors are also involved in the variability in antidepressant response, by way of molecular pathways linked to neuronal signalling pathways and neuroplasticity (Abelaira et al., 2014). Evidence from infectious disease pharmacotherapy shows that HLA-B*57:01 allele screening is effective in preventing severe hypersensitivity reactions to antiretroviral drug abacavir in patients with HIV infection (Dean 2018). Pharmacogenomic test has thus become an integral part of safe antiretroviral therapy by identifying people at risk of immune-mediated drug toxicity (Sousa-Pinto et al., 2015).

Additional therapeutic areas have also benefited from pharmacogenomic research, such as in gastroenterology, where the presence of the TPMT and NUDT15 polymorphisms is strongly linked to thiopurine-induced leukopenia in patients with inflammatory bowel disease (Grover et al., 2021). Identification of these variants in the genes enables doctors to adjust the dose of thiopurine and lower the risk for severe haematological toxicity during immunosuppressive therapy (Walker et al., 2019). In pain management, variants in the CYP2D6 enzyme are important for the metabolism of opioid analgesic drugs and explain some of the variability in analgesic efficacy and adverse effects in patients (Ballester et al., 2022). Neurological pharmacogenomics has also shown that mouth neurological pharmacogenomics can play a role in the response to anti-epileptic drugs and in the susceptibility to developing severe cutaneous adverse reactions (Borowicz-Reutt et al., 2023). These findings together outline the increasing clinical significance of pharmacogenomic testing in a variety of therapeutic fields where there are observed genetic effects on the response to pharmacologic therapy.

Despite these improvements, the implementation of pharmacogenomic knowledge into actual clinical practice is still inconsistent across healthcare systems across the world (Klein et al., 2017). Difficulty in implementation is usually constrained by barriers such as poor awareness by clinicians, poor access to genetic testing infrastructure and confusion over how to interpret pharmacogenomics data in clinical settings (AL-Eitan & Tarkhan, 2016). Economic considerations are also important to the adoption of pharmacogenomic testing, especially in low- and middle-income healthcare systems in which cost-effectiveness considerations are crucial (Klein et al., 2017). Another key challenge is the minority representation of diverse populations in pharmacogenomic research studies, which can lead to decreases in the generalizability of genomic research findings across global populations (Popejoy, 2019). Responding to these limitations is through coordinated efforts on an international scale and supporting genomic diversity in terms of research, available clinical guidelines, and, in the case of healthcare professionals, through better education. Continued advances in the understanding of pharmacogenomics and developments in genomic technologies are expected to further reinforce the use of personalised medicine and enhance the safety and efficacy of pharmacotherapy (Sadee et al., 2023). Therefore, a thorough assessment of current pharmacogenomic advances and clinical applications is necessary in order to promote the wide implementation of precision therapeutics in contemporary healthcare systems.

Objectives of the review

The goal of this review is to review the recent progress made in the field of pharmacogenomics and its contribution to the establishment of personalised medicine. It aims to provide a summary of current knowledge of genetic factors affecting drug response and indicate key clinical applications in several therapeutic areas. The review also relates challenges in clinical implementation of pharmacogenomic testing and explores future directions in using genomic information in the clinical setting.

Review

3.1 Pharmacogenomics in Oncology

Pharmacogenomics has had a major impact in the field of cancer treatment, allowing for a personalised approach to treatment that is based on the genetic profile of the specific tumour and patient (Sadee et al., 2023). Advances in genomic technologies have made it possible to detect molecular biomarkers that predict therapeutic response, resistance and toxicity to drugs, increasing the precision of cancer treatments (Cecchin & Stocco, 2020). Tumour heterogeneity and genetic alterations are important determinants of the effectiveness of anticancer treatment, which has led to the development of targeted therapies guided by specific genetic mutations (Camidge et al., 2019). Pharmacogenomic biomarkers like epidermal growth factor receptor (EGFR), human epidermal growth factor receptor-2 (HER2) and KRAS mutations have been widely applied in facilitating treatment decision-making in a number of cancer types (Wu & Qu, 2015). These biomarkers help clinicians to choose therapies that target oncogenic pathways that are causing tumour progression and survival (Camidge et al., 2019).

Targeted therapies are one of the best examples of the application of pharmacogenomics in cancer treatment due to the fact that targeted therapies target molecular abnormalities specific to cancer cells and have minimal impact on normal tissues (Piawah & Venook, 2019). For example, mutations in the epidermal growth factor receptor (EGFR) have been found to be predictive of the efficacy of tyrosine kinase inhibitor treatment in non-small cell lung cancer, leading to better therapeutic outcomes and outcomes (Camidge et al., 2019). Similarly, overexpression or amplification of HER2 in breast cancer is employed to identify patients who may benefit from HER2-targeted monoclonal antibody therapies such as trastuzumab (Wu & Qu, 2015). In colorectal cancer, mutations in the KRAS gene play a role in response to anti-EGFR monoclonal antibodies and patients with mutations in the KRAS gene are usually not helped by these medications (Piawah & Venook, 2019). These findings show the importance of molecular diagnostics in drug therapy decisions to promote clinical results in the case of oncology.

The use of next-generation sequencing has further increased the pace of discovery of pharmacogenomic biomarkers and enabled the complete genomic profiling of tumours (Morganti et al., 2019). Several actionable mutations can be identified at the same time using genome-wide analyses, and clinicians can make treatment choices tailored to the molecular tumour profile of patients (Morganti et al., 2019). This approach has helped in the emergence of precision oncology in which treatment selection has become more dictated by genomic information as opposed to just focused on the tumour histology (Sadee et al., 2023). Pharmacogenomics is also involved in predicting adverse drug reactions, which are associated with chemotherapy and targeted therapies, and permits clinicians to adjust dosing strategies to reduce toxicity related to the therapeutic treatment (Cascorbi, 2018). As genomic technologies continue to evolve, pharmacogenomic testing is likely to become an integral part of the cancer diagnosis, treatment planning and therapeutic monitoring in modern oncology practice. Table 1 shows important pharmacogenomic biomarkers and drug associations in personalised medicine.

Table 1. Key Pharmacogenomic Biomarkers and Associated Drugs

Gene/Biomarker	Drug	Clinical Application	Therapeutic Area	Reference
EGFR mutation	Gefitinib	Predicts response to tyrosine kinase inhibitors	Oncology	(Camidge et al., 2019)
HER2 amplification	Trastuzumab	Guides targeted therapy in HER2-positive tumours	Oncology	(Wu & Qu, 2015)
KRAS mutation	Cetuximab	Predicts resistance to anti-EGFR therapy	Oncology	(Piawah & Venook, 2019)
CYP2C19	Clopidogrel	Influences the antiplatelet drug activation	Cardiovascular	(Brown & Pereira, 2018)
VKORC1	Warfarin	Determines warfarin dose requirements	Cardiovascular	(Kimmel et al., 2013)
SLCO1B1	Statins	Associated with statin-induced myopathy risk	Dyslipidemia	(Maxwell et al., 2017)
CYP2D6	Codeine	Affects opioid metabolism and analgesic response	Pain management	(Ballester et al., 2022)
HLA-B*57:01	Abacavir	Predicts hypersensitivity reactions	Infectious disease	(Dean, 2018)
TPMT	Azathioprine	Predicts risk of myelosuppression	Gastroenterology	(Grover et al., 2021)
NUDT15	Thiopurines	Associated with leukopenia risk	Gastroenterology	(Walker et al., 2019)

3.2 Pharmacogenomics in Cardiovascular Therapy: Anticoagulants

Pharmacogenomics has gained increasing importance in the field of cardiovascular medicine, especially in the optimization of blood coagulation treatment where genetic variability plays a major role in the metabolism of drugs and their use (Cascorbi, 2018). Warfarin, one of the most widely prescribed oral anticoagulants for the prevention thromboembolic events, has a lot of interindividual variability in doses required because of genetic and clinical factors (Asiimwe et al., 2021). Variants in genes coding for the enzymes involved in warfarin metabolism especially CYP2C9 as well as polymorphisms in the vitamin K epoxide reductase complex gene VKORC1 have important roles in determining patient sensitivity to the drug (Kimmel et al., 2013). Individuals who are carriers of reduced function CYP2C9 alleles metabolize warfarin at a slower rate, therefore raising the risk of bleeding complications when standard dosing regimens are applied.10 Asiimwe et al. Similarly, genetic polymorphisms of VKORC1 influence pharmacodynamic response to warfarin by altering the target enzyme of the drug and influence the need for maintenance dose for effective anticoagulation (Kimmel et al., 2013).

Pharmacogenomic-guided dosing algorithms have therefore been developed to combine information from the genetic analysis with clinical factors such as the age, body weight and concomitant medications to predict appropriate warfarin dosing (Asiimwe et al., 2021). These algorithms help improve the prediction accuracy of doses and facilitate the reduction of the time required to attain a stable anticoagulation in patients receiving warfarin therapy (Kimmel et al., 2013). Clinical studies have shown that genotype-guided dosing orders may improve the safety of therapy by reducing the potential impact of hemorrhagic complications, as well as reducing the risk of subtherapeutic anticoagulation (Bjorkest et al., 2016). Despite these benefits, implementing pharmacogenomic tests for anticoagulant therapy on a routine basis is currently not widely practised across healthcare systems because of important logistical, economic, and clinical considerations (Klein et al., 2017). Continued research and incorporation of pharmacogenomic data and drug treatment into clinical guidelines may lead to further improvements in the safety and efficacy of anticoagulant therapies in the management of cardiovascular disease. Genetic and clinical determinants affecting anticoagulant therapy response. Figure 1.

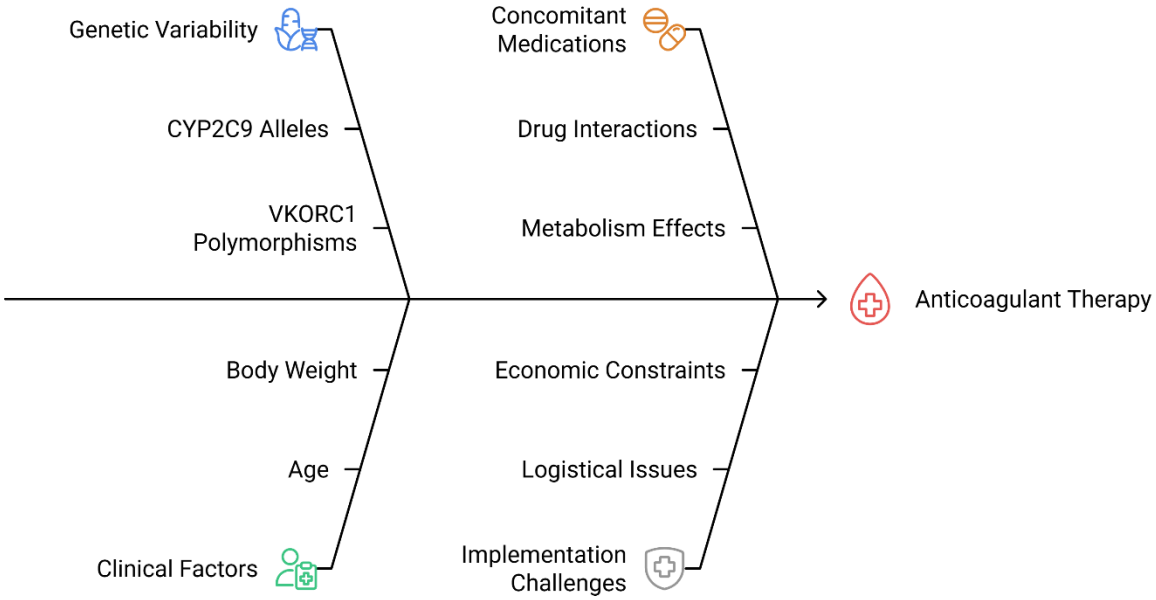

Figure 1: Factors Influencing Pharmacogenomic-Guided Anticoagulant Therapy

3.3 Pharmacogenomics in Cardiovascular Therapy: Antiplatelet Drugs

Pharmacogenomics is an important component in optimising antiplatelet therapy, especially in patients who are prescribed clopidogrel for the prophylaxis and treatment of cardiovascular thrombotic events (Brown & Pereira, 2018). Clopidogrel is a prodrug that needs metabolic activation mainly by the cytochrome P450 enzyme CYP2C19, and genetic polymorphisms in the cytochrome P450 enzyme CYP2C19 play an important role in modifying the antiplatelet activity of the clopidogrel (Karaźniewicz-Łada et al., 2014). People with loss-of-function CYP2C19 alleles have a lower rate of conversion of clopidogrel to its active metabolite, resulting in reduced platelet inhibition and a higher risk of adverse cardiovascular outcomes (Brown & Pereira, 2018). Clinical studies have revealed that people with decreased metabolic capacity of CYP2C19 have a higher incidence of major adverse cardiovascular events when treated with standard clopidogrel therapy following acute coronary syndromes or percutaneous coronary interventions (Doll et al., 2016).

Genetic testing for CYP2C19 variants has therefore become a topic of interest as a way to guide antiplatelet therapy to improve treatment outcomes for cardiovascular patients (Cascorbi, 2018). Identification of poor or intermediate metabolizers enables the clinician to consider alternative antiplatelet (e.g., prasugrel or ticagrelor, which are not too dependent on CYP2C19 metabolism-mediated activation) agents (Doll et al., 2016). Pharmacogenomic-guided therapy has been suggested as a means of lowering individuals at genetic risk of treatment failure due to inadequate platelet

inhibition (Brown & Pereira, 2018). Furthermore, aiding in the integration of pharmacogenomic testing into clinical decision-making may further help improve risk stratification and help to provide more individualised management of antiplatelet therapy in patients undergoing cardiovascular interventions (Chenoweth et al., 2020). Despite a growing body of evidence in favour of the clinical utility of CYP2C19 genotyping, routine use in the clinic setting is variable, as awareness of the technique remains low, inconsistent guideline recommendations exist, and there are concerns about the cost-effectiveness of pharmacogenomic testing (Klein et al., 2017).

3.4 Pharmacogenomics of Statins and Dyslipidemia Treatment

Pharmacogenomics has grown in importance in the management of dyslipidemia owing to the impact that genetic variability may exert on efficacy and safety of lipid-lowering therapies, and especially statins (Maxwell et al., 2017). Statins are currently the first-line pharmacological treatment for hyperlipidemia and cardiovascular risk reduction; however, significant interindividual differences in response to the drug treatment and adverse effects have often been noted among patients receiving these drugs (Ahn & Choi, 2015). Genetic polymorphisms of drug metabolism, transport and cellular uptake contribute to these variations and may help to determine the treatment outcome in clinical practice (Sivkov et al., 2021). One of the most widely studied pharmacogenomic factors known to be linked to statin treatment is the SLCO1B1 gene, which is responsible for the hepatocyte transporter OATP1B1 that is responsible for the uptake of statins into liver cells (Maxwell et al., 2017).

Variants in the SLCO1B1 gene have been associated with differences in the pharmacokinetics of statins and with an elevated risk of statin-induced myopathy, an important adverse effect that can reduce the tolerability of statin treatment (Maxwell et al., 2017). Patients with reduced-functional alleles of SLCO1B1 have a reduced hepatic uptake of statins, leading to a higher plasma concentration of the drug and an increased risk of muscle toxicity (Sivkov et al., 2021). Identification of such genetic variants enables clinicians to optimise the type and/or dosage of statins to minimise adverse effects and yet ensure the lipid-lowering effect is maintained (Cascorbi, 2018). Pharmacogenomic testing may thus help to choose the most appropriate therapy with statins for each patient on the basis of their genetic profile.

Beyond statins, new lipid-lowering medications such as PCSK9 inhibitors and new medications aimed at cholesterol metabolism have led to an expansion in the scope of personalised treatment strategies of dyslipidemia (Ahn & Choi, 2015). Continued research into genetic determinants of lipid metabolism and response to drugs can be expected to help enhance individual therapeutic approaches and optimize reduction in cardiovascular risk based on pharmacogenomics-guided therapy.

3.5 Pharmacogenomics in Psychiatric Disorders: Antidepressants

The role of pharmacogenomics has become more and more important in psychiatric medicine due to the large variability in response to antidepressant medications among patients (Pardiñas et al., 2021). Antidepressant therapy is the most common treatment strategy used in the treatment of major depressive disorder, a significant proportion of patients do not experience adequate remission of symptoms with initial treatment strategies (Willner et al., 2013). Genetic factors such as drug metabolism, neurotransmitter pathways and neuronal signalling contribute to the variation in antidepressant efficacy and adverse drug reactions among individuals (Abelaira et al., 2014). Polymorphisms in genes that code for cytochrome P450 enzymes, especially CYP2D6 and CYP2C19, play a major role in determining the rate of metabolism of many frequently prescribed antidepressants (Pardiñas et al., 2021).

People with reduced-function versions of the enzymes tend to metabolise antidepressants more slowly, leading to higher plasma levels of these drugs and a higher risk of adverse effects (Cascorbi, 2018). On the other hand, people with ultrarapid metabolizer genotypes may metabolise medications faster, which can result in subtherapeutic levels and lower clinical effectiveness (Pardiñas et al., 2021). Pharmacogenomic testing for CYP2D6 and CYP2C19 variants has therefore been put forward as a strategy to inform the choice of antidepressant and dosing to optimise treatment outcomes (Chenoweth et al., 2020). Genomic information incorporated into prescribing decisions may help clinicians determine which patients have a greater likelihood of responding to certain antidepressants that may also lead to treatment-related toxicity.

In addition to metabolic genes, molecular pathways that are involved in neuronal plasticity and intracellular signalling have also been implicated in antidepressant response (Abelaira et al., 2014). Epigenetic mechanisms that control gene expression may also have an additional impact on antidepressant efficacy by modulating neurobiological processes that are involved in the regulation of mood (Vialou et al., 2013). Continued improvements in pharmacogenomic studies may therefore play a role in bringing about better, individualised treatments for depressive disorders and improving outcomes on therapeutics administered in psychiatric treatment. Figure 3 Genetic and epigenetic factors that affect pharmacogenomic responses in psychiatric medicine.

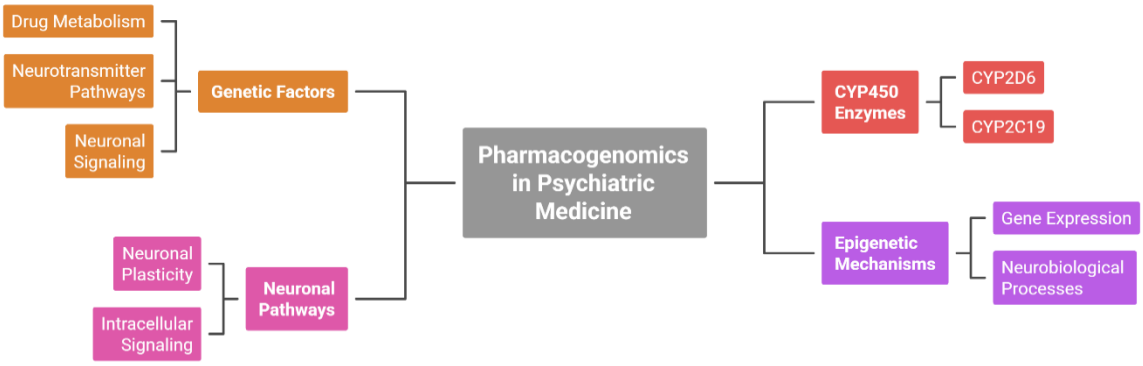

Figure 2: Pharmacogenomics in Psychiatric Medicine

3.6 Pharmacogenomics in Psychiatric Disorders: Antipsychotic Therapy

Pharmacogenomics has an important role in understanding variability in response to antipsychotic medications used for the treatment of schizophrenia and related psychotic disorders (Pardiñas et al., 2021). Antipsychotic therapy is the most common pharmacologic treatment for schizophrenia, but clinical responses vary greatly within patients because of the varying levels of drug metabolism, sensitivity, and neurobiological pathways (Harrow & Jobe, 2013). Genetic polymorphisms that affect drug-metabolising genes, such as those in the cytochrome P450 family (e.g. CYP 2D6), affect the pharmacokinetics of a number of antipsychotic drugs (e.g. Cascorbi, 2018). Variations in these enzymes can modify plasma drug concentrations, which can result in variations in the effectiveness of treatment, or an elevated risk of adverse reactions in persons receiving similar treatment regimens (Pardiñas et al., 2021).

In addition to metabolic genes, pharmacodynamic factors also contribute to the variability in antipsychotic response. In addition to metabolic genes, the pharmacodynamics factors are also contributing to the variability in antipsychotic response, such as a genetic variation in dopamine and serotonin receptor pathways that regulate the neurotransmission in the central nervous system (Pardiñas et al., 2021). These genetic influences can impact the extent of the improvement of symptoms during antipsychotic treatment as well as the predisposition to adverse drug reactions (Yogaratnam et al., 2013). One of the most common problems that happens in response to long-term treatment with antipsychotic drugs is disturbance of metabolism, such as weight gain, dyslipidemia, and insulin resistance, that may be due in part to genetic susceptibility interacting with drug exposure (Yogaratnam et al., 2013).

Pharmacogenomic testing may therefore aid in more tailored treatment strategies, either by determining which patients may be more prone to respond to particular antipsychotic drugs or who may be more prone to adverse drug reactions (Chenoweth et al., 2020). Integration of genetic information into psychiatric practice could lead to better choice of treatment, fewer adverse effects and better long-term outcome for individuals with psychotic disorders.

3.7 Pharmacogenomics of Antiepileptic Drugs

Pharmacogenomics has made a big contribution to the understanding of the variability in therapeutic response and adverse drug reactions associated with antiepileptic medications used in the treatment of epilepsy (Borowicz-Reutt et al., 2023). Epilepsy is a complex neurological condition that is characterised by recurrent seizures, and although antiepileptic drugs are effective in many patients, a significant percentage of these patients demonstrate drug resistance or treatment-related toxicity (Catterall, 2014). Genetic factors affecting neuronal ion channels, drug metabolism and immunological-mediated reaction have a significant role in the determination of individual responses to antiepileptic therapy (Borowicz-Reutt et al., 2023). Variations in genes for sodium channels and other targets in neurons may influence the pharmacodynamic response to certain antiepileptic drugs and contribute to differences in seizure control of patients (Catterall, 2014).

Pharmacogenomic research has also shown the presence of genetic markers linked to serious adverse drug reactions to certain antiepileptic drugs (Mullan et al., 2019). Among those, alleles of human leukocyte antigen (HLA) have been reported to be strongly linked to drug-induced hypersensitivity reactions, especially severe cutaneous adverse reactions such as Stevens-Johnson syndrome and toxic epidermal necrolysis (Mullan et al., 2019). For example, certain variants in the HLA gene are known to make people more susceptible to a hypersensitivity to the effect of certain drugs such as carbamazepine and other aromatic anti-epileptic agents (Borowicz-Reutt et al., 2023). Identification of these genetic risk factors has allowed the use of pharmacogenomic screening strategies in some clinical settings to avoid life-threatening adverse drug reactions (Mullan et al., 2019).

The integration of pharmacogenomic testing in the management of epilepsy may therefore provide better results by approaching the drug selection to reduce the risk of severe toxicity (Cascorbi, 2018). As genomic technologies continue to improve, it is likely that pharmacogenomics will play a greater role in an individual's treatment for epilepsy.

3.8 Pharmacogenomics in Pain Management and Opioid Therapy

Pharmacogenomics has been playing an ever-growing role in understanding the individual response to opioid analgesics in the management of acute and chronic pain (Ballester et al., 2022). Opioids such as codeine, tramadol and oxycodone are frequently prescribed for pain relief, but there are significant differences in analgesic efficacy and susceptibility to

adverse effects between patients (Paul et al., 2021). Genetic variation in drug-metabolising enzymes is a major factor in the opioid pharmacokinetics and in the therapeutic response among individuals (Ballester et al., 2022). In particular, polymorphisms in the cytochrome P450 family of enzymes (CYP2D6) are a significant influence on the metabolism of several opioids, affecting their metabolism by converting prodrugs into active analgesic metabolites (Ballester et al., 2022).

Patients with reduced-function alleles of CYP2D6 are referred to as poor metabolizers and may have inadequate analgesic effects due to reduced formation of active opioid metabolites (Cascorbi, 2018). On the other hand, people who carry several copies of the gene CYP2D6 are referred to as ultrarapid metabolizers and are likely to create more active metabolites, thus raising the likelihood of opioid toxicity and respiratory depression (Ballester et al., 2022). These pharmacogenomic differences stress the significance of heredity in choosing both the safety and the usefulness of triggers like opioids in clinical practice (Paul et al., 2021).

Pharmacogenomic testing has therefore been suggested as a strategy to guide opioid choice and doses to achieve optimal analgesia and a minimum of adverse drug reactions (Chenoweth et al., 2020). Integrating genetic information with pain management can potentially enable clinicians to identify candidates who will likely respond well to particular opioid drugs or otherwise require an alternate approach to pain management (Ballester et al., 2022). Continued development in pharmacogenomics may help the development of personalised approaches to the management of pain, which will improve therapeutic outcomes and decrease the risks of opioid-related complications in the clinical management of pain.

3.9 Pharmacogenomics in Infectious Disease Therapy

Pharmacogenomics is of growing importance in the management of infectious diseases since genetic variability can determine drug efficacy and the risk of adverse drug reactions during antimicrobial treatment (Biswas et al., 2022). Differences in immune responses, drug metabolism, and pharmacodynamics interactions mediated by host genetic factors can account for differences in treatment outcomes for patients receiving the same drug therapy in the same manner (Chenoweth et al., 2020). One of the most well-known examples of pharmacogenomics in the treatment of infectious diseases includes the correlation between the HLA-B57:01 allele and hypersensitivity responses to the antiretroviral treatment abacavir (Dean, 2018). Abacavir is popularly used in combination antiretroviral therapy in the treatment of human immunodeficiency virus (HIV) infection; however, those individuals who have the HLA-B57:01 allele have a significant risk increase for the development of severe immune-mediated hypersensitivity reactions (Sousa-Pinto et al., 2015). Pharmacogenomic screening for this allele before starting abacavir treatment has therefore become a routine clinical procedure that seeks to avoid potentially life-threatening adverse reactions in susceptible patients (Quiros-Roldan et al., 2020).

To develop a new generation of infectious disease therapy by integration of pharmacogenomic testing into the clinical treatment approach led to drug safety and contributed to the personalisation of the treatment approach (Biswas et al., 2022). Together with HIV therapy, genetic factors may also be relevant in determining response to anti-infective drugs used to address emerging infectious diseases and thus serve as an example of the relevance of pharmacogenomics in infectious diseases treatment (Biswas et al., 2022). Advances in genomic research have helped identify host genetic variants linked to drug response and toxicity and may contribute to the development of a personalised approach to infectious disease therapy (Chenoweth et al., 2020). Incorporating pharmacogenomic information into treatment guidelines and clinical decision-making could therefore lead to an increase in the effectiveness of therapy, improvements in patient safety, and support the implementation of precision medicine in the therapy of infectious diseases across a wide range of healthcare settings. Host genetic factors in infectious disease therapy outcomes are shown in Figure 2.

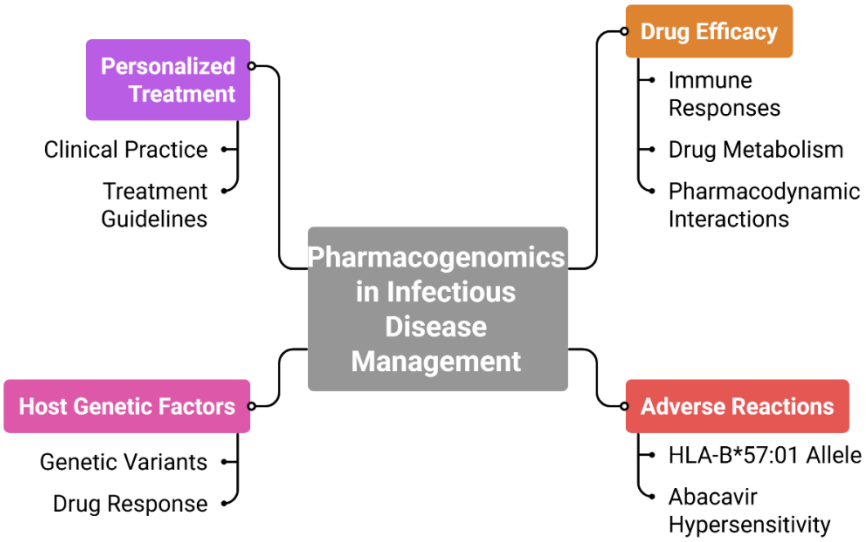

Figure 2: Pharmacogenomics in Infectious Disease Management

3.10 Pharmacogenomics of Immunomodulatory and Gastrointestinal Drugs

Pharmacogenomics has an important role to play in optimising therapy with immunomodulatory drugs used in gastrointestinal disorders, specifically in the treatment of inflammatory bowel disease, where thiopurine medications are widely prescribed (Grover et al., 2021). Thiopurines, e.g. azathioprine, 6-mercaptopurine, are often used as immunosuppressive drugs; however, considerable interindividual variability exists between response to therapy and risk of developing adverse drug effects (Walker et al., 1995). Genetic polymorphisms in drug metabolism are important determinants of thiopurine-related adverse reactions, especially severe myelosuppression that may occur in therapy (Asada et al., 2016). Variants in the thiopurine S-methyltransferase (TPMT) gene decrease the activity of this enzyme and result in the accumulation of metabolites of active thioguanine, with an increased risk of developing haematological toxicity in susceptible individuals (Grover et al., 2021).

Another key genetic factor that affects the safety of thiopurines is the NUDT15 gene, which codes for an enzyme that is involved with detoxifying the thiopurine metabolites in cells (Walker et al., 2019). Mutations in NUDT15 have been linked firmly to thiopurine-induced early leukopenia development in patients with such therapy and are more common in Asian populations, where NUDT15 gene variants are more abundant than in other populations (Asada et al., 2016). Identification of TPMT and NUDT15 polymorphisms using pharmacogenomic testing allows clinicians to adjust the dosage of a medication or choose alternative medications in order to reduce treatment-related toxicity (Grover et al., 2021). Incorporation of pharmacogenomic screening into routine clinical practice, therefore, endorses the notion of safer and more individualised use of immunomodulatory drugs in gastrointestinal problems.

Beyond the thiopurine therapy, pharmacogenomic studies have also drawn attention to the wider scope of genetic testing for directing drug development and therapeutic strategies for personalised medicine. (Gupta, 2015) Understanding genetic variations in drug response can help in the more accurate choice of treatment and better clinical outcomes for patients taking immunomodulatory medications (Raj, 2019). Continued research in the field of pharmacogenomics is therefore expected to increase the use of individualised treatment approaches in gastrointestinal and inflammatory diseases. Table 2 shows therapeutic uses of pharmacogenomics and important genetic markers for drug response in personalised medicine.

Table 2. Clinical Applications of Pharmacogenomics in Major Therapeutic Areas

Therapeutic Area	Drug Class	Key Genetic Marker	Clinical Benefit	Reference
Oncology	Targeted anticancer drugs	EGFR, HER2	Selection of effective targeted therapy	(Camidge et al., 2019)
Cardiovascular diseases	Anticoagulants	VKORC1, CYP2C9	Optimised warfarin dosing	(Asiimwe et al., 2021)
Cardiovascular diseases	Antiplatelet drugs	CYP2C19	Improved antiplatelet therapy selection	(Brown & Pereira, 2018)
Dyslipidemia	Statins	SLCO1B1	Prevention of statin-induced toxicity	(Maxwell et al., 2017)
Psychiatry	Antidepressants	CYP2D6, CYP2C19	Improved antidepressant efficacy	(Pardiñas et al., 2021)
Psychiatry	Antipsychotics	Dopamine receptor genes	Personalised schizophrenia treatment	(Yogaratnam et al., 2013)
Neurology	Antiepileptic drugs	HLA variants	Prevention of severe cutaneous reactions	(Mullan et al., 2019)
Pain management	Opioids	CYP2D6	Optimised analgesic response	(Ballester et al., 2022)
Infectious diseases	Antiretrovirals	HLA-B*57:01	Prevention of hypersensitivity reactions	(Sousa-Pinto et al., 2015)
Gastroenterology	Thiopurines	TPMT, NUDT15	Reduced risk of hematologic toxicity	(Grover et al., 2021)

Limitations and Future Directions

Despite the large advances, there are a few limitations to the broad implementation of pharmacogenomics in the clinical setting. Many pharmacogenomic associations have been found in certain populations, which causes the generalisability of results across different ethnic groups. Limited knowledge among clinicians, inadequate training in genomic medicine, and no standardised clinical guidance also limit the regular use of pharmacogenomic testing. Economic barriers, such as the cost of genetic testing and poor health care infrastructure in developing regions, have an impact on accessibility, too. In addition, however, complex gene-drug interactions and the role of environmental and lifestyle factors make pharmacogenomic data difficult to interpret in a clinical setting.

Future studies should aim to broaden large-scale multiethnic genomic studies for more reliable and broader global applications of pharmacogenomic results or findings. Integration of pharmacogenomic information into the electronic health record and clinical decision support systems may support its routine implementation in the health care setting. Improvements in artificial intelligence, machine learning, and multi-omics technologies can be expected to improve the

predictive capabilities for drug response or treatment outcomes. Continued development of clinical guidelines, physician education initiatives, and cost-efficient strategies for genomic testing will further nurture integration of precision medicine strategies using pharmacogenomics and more effective individual therapeutic approaches.

Conclusion

This review highlights the expanding role of pharmacogenomics in advancing personalised medicine by examining how genetic variability influences drug response, therapeutic efficacy, and treatment safety. Pharmacogenomic research has provided significant insights into gene–drug interactions across multiple clinical areas, including oncology, cardiovascular diseases, psychiatry, neurology, infectious diseases, and gastrointestinal disorders. Identification of genetic biomarkers has improved the ability to predict treatment outcomes and has supported the development of targeted and individualised therapeutic strategies. These advances demonstrate how pharmacogenomics contributes to optimising drug selection, dosage adjustment, and prevention of adverse drug reactions in modern clinical practice. At the same time, several challenges continue to limit the widespread integration of pharmacogenomics into routine healthcare. Variability in clinical guidelines, limited genomic literacy among healthcare professionals, and the high cost of genetic testing remain important barriers in many healthcare systems. In addition, the underrepresentation of diverse populations in pharmacogenomic studies may restrict the generalizability of existing findings. Addressing these issues through expanded research, improved clinician education, and integration of pharmacogenomic data into clinical decision-support systems will be essential for broader implementation. Continued progress in genomic technologies and precision medicine approaches is expected to further enhance the clinical value of pharmacogenomics and support the development of safer and more effective individualised therapies.

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